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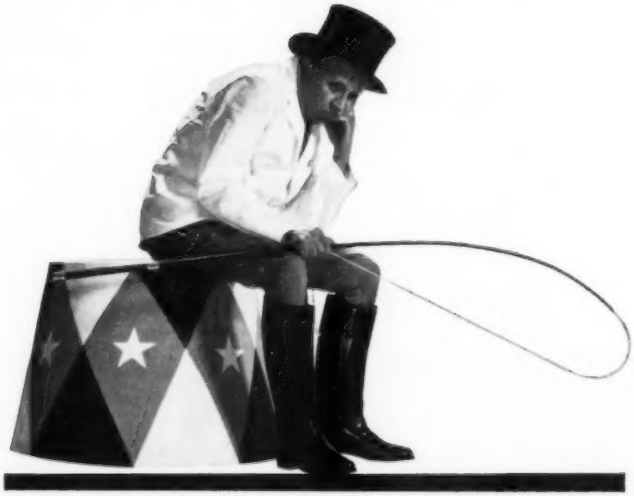
American Journal of Pharmacy

Published monthly by the Philadelphia College of Pharmacy and Science
43d Street, Kingsessing and Woodland Avenues, Philadelphia 4, Pa.

Annual Subscription $4.00 — Foreign Postage, 25 Cents Extra
Single Numbers, 40 Cents — Back Numbers, 50 Cents

Second Class Postage Paid at Philadelphia, Pa.



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AND THE SCIENCES SUPPORTING PUBLIC HEALTH

Since 1825

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Vol. 133 FEBRUARY 1961 No. 2

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EDITORIAL

CARCINOGENS, HYSTERIA, AND LOGIC

THE current efforts by the Food and Drug Administration, acting in conformity with the wishes of Congress, to ban all potentially carcinogenic dyestuffs for use on or by the public are largely sound although we suspect somewhat influenced by public hysteria. In the case of certain of the dyes which have been banned, the animal experiments which demonstrated them to be carcinogenic bear little or no relationship to the manner or amount in which these dyes have been used. Nevertheless, we believe that it is better to be safe even though inconvenient than to permit a risk of carcinogenicity in humans which cannot very well be measured.

The ironic thing about these new regulations is the clear evidence of gross inconsistency with which Congress—and, indeed, the public at large—faces the over-all problem of cancer and its prevention. An objective, impartial, and unprejudiced evaluation of human behavior would surely lead to the conclusion that the exercise of logic among humans is a rarity and, in this case, it most certainly does not apply. In the new regulations, we see an effort to rule out substances where there is no clear-cut proof that they have ever caused human cancer and, yet, we see no similar effort to ban or even restrict the use of that which undoubtedly is the chief cause of lung cancer in man; namely, the smoking of cigarettes. The reason for this inconsistency is not difficult to assess. Proscribing the use of certain dyes works a hardship on only a relatively few people in the formulation of food, drugs, and cosmetics. Since they are in such a small minority, the hew and cry which they have raised can be ignored or answered only with the succinct statement that no potential carcinogen can be tolerated. In the case of cigarettes where all of the evidence is so convincing and damaging, any effort to restrict their use would lead to a public outcry of the first magnitude. One, therefore, cannot help but be led to the conclusion that in our actions we are governed not by what is right, necessarily, but only when the stand taken is likely to be a popular one. From the standpoint of logic, a

thing which is wrong even though it may be multiplied by a factor of 50 million is not only still wrong but tremendously more so, and the fact that 50 million people prefer to increase their likelihood of developing lung cancer by a factor of several hundred per cent still leaves the risk of cancer a serious one and the disease just as terrible.

Not only does our government do nothing to discourage smoking, it even encourages the practice by assisting the tobacco farmer financially just as if he were producing something which fills a basic human need as does food. There is, of course, also the tremendous tax revenue of tobacco products to be considered, as we suspect it is.

We suppose it is too much to expect that government, which is but a reflection of our own strengths and weaknesses, would do that which truth and logic dictate. There is, however, something to be said to those few individuals who indeed do "think for themselves." Even these—if we believe some of the current cigarette advertising—after careful deliberation, still choose cancer.

L. F. Tice

GAS CHROMATOGRAPHY—A POTENTIAL METHOD IN PHARMACEUTICAL ANALYSIS

By Gunnar Gjerstad *

THE entire field of chromatography is a rapidly developing one. It was only a few years ago that absorption phenomena were just an annoying and not at all understood obstacle encountered in attempts to secure high vacuums or to recover small amounts of substances from solutions. However, a careful examination of these phenomena has converted this nuisance into one of the invaluable techniques for all chemical analysts. Liquid-solid chromatography, paper chromatography, and paper electrophoresis are now well-established methods for the separation, purification, and identification of several types of solid substances which are encountered in daily laboratory work. Ion-exchange columns are now very commonly employed in all scientific laboratories.

All of the above methods are limited to solid substances and the separation of gases or low-boiling liquids was considered possible only by fractionate distillation, which presents distinct and well-known limitations.

However, in 1952, James and Martin (the latter in the previous year received the Nobel Prize for his development of the paper chromatographical technique) came up with a method suitable for the chromatographic separation of *gases*. Since that time, numerous improvements of the methods have been reported.

Gas chromatography is the designation for a separation method for microquantities in which the mobile phase is a gas, the stationary phase is either solid or a liquid, and termed "gas absorption chromatography" and "gas liquid partition chromatography" (G. L. P. C.), respectively. The British designate it "vapour-phase chromatography." Chromatography is a definite misnomer in this connection since no *color* is involved.

The following is intended to merely introduce you to this most recent innovation, in as simple terms as possible, avoiding any high-flying physico-mathematical equations which are necessary for explanation of the more intricate theories involved. It should be stressed that the method is not limited to gases only, but may be applied in the analysis of liquids or liquid mixtures with a boiling point up to

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300°C., hence has great potential in the analysis of the complex volatile oils.

A rather involved apparatus is needed for gas chromatography. Commercial streamlined models sell for around $3,000-$10,000, but adept analysts may build parts of the apparatus, reducing the total cost of this versatile apparatus to below $1,000. The only parts which it is advisable to purchase are the electronic gadgets.

The main parts of a gas chromatograph are a thermostat, enclosing a long column and a detector, and an injection chamber (see Fig. 1). The theory behind the apparatus is rather involved, and it

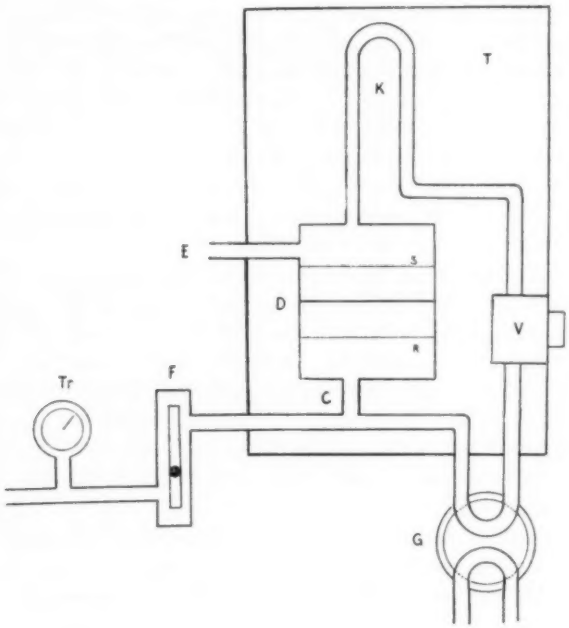

FIGURE 1

Sketch of a gas chromatograph. T, thermostat; K, column; D, detector; R, S, metal wires coupled in a Wheatstone bridge; V, injection chamber for liquid substances. G, gas dosimeter; Tr, pressure valve; F, velocity gauge (after Gjaldbaek).

may not be necessary for us to know the inner secrets of the apparatus since it would be unwise to try to repair the apparatus if it should break down for some reason.

The main principle of its function is based on the fact that heat is conducted away from a hot body situated in a gas, at a rate depending upon the nature of the gas, other factors being constant. This difference in conductance is measured in a katharometer (detector) which is the tender portion of the apparatus and which functions as a resistance thermometer. It is composed of two separate rooms which are equipped with two metal wires coupled in a Wheatstone bridge. Changes in resistance are strongly amplified and transferred to an automatic oscillograph. These two wires lose heat mainly by convection, and their temperature resistance to current will be dependent on the heat conduction properties of the gas surrounding them. The only thing an analyst has to do is to inject the substance for analysis into the column. Liquids with boiling points below 300° or the gas can be measured with a micro pipette and injected by means of a hypodermic syringe through a membrane of rubber. This device resembles very much the ordinary penicillin vials for injection. The amounts of substance needed are extremely small, from .001 to a *maximum* of .05 milliliters.

After the sample has been introduced, a continuous flow of inert gas from a bomb is pressed through the tube system of the apparatus. The column in which the gas is partially absorbed and distributed may be of various compositions. This will be discussed later. The supporting phase is contained in a copper tube of ½ centimeter in diameter and a length of 5 yards. This would make the apparatus rather cumbersome extending through several floors. To avoid that, the copper tube is bent several times or also often arranged in the form of a coil.

The most advantageous carrier gas from a thermodynamic point of view is hydrogen. However, this gas is rarely used since it is, of course, highly combustible and explosive. In all experiments I have seen reported or done, helium is the gas used.

The gas from a commercial cylinder is first passed through a couple of drying towers to make it completely water free and through a trap for the absorption of carbon dioxide. It is of paramount importance that the apparatus be kept at a constant temperature, usually above 200°. The operating temperature may vary, and is not crucial

as long as it is *constant* and above that of the highest boiling fraction. This involves the biggest problem, namely that of heat insulation. A highly sensitive thermostat device is consequently indispensable.

The time required for exhaustive analysis of very complex gas or liquid mixtures is from ten minutes to one hour depending upon the complexity of substance and the speed of gas flow.

The Column

A wide variety of solids may be used as the supporting phase. In the classical experiment, acid-washed Celite was used. Today, various other silicates are still very popular; any thermostable, absorbent powder may be used.

An important requirement is the particle size which must be uniform from 10-300 μ. The difficulty in setting up the apparatus is to obtain a uniform packing. Very good results have been obtained by use of screen fractions of ground fire-brick, commercial products being the German made Sterchamol ® and John Manville firebrick C22 ®. The highest efficiency, *viz.* the best compromise between small particle size and absence of channeling, has been found in most instances and columns to be particles between 200 and 500 μ. The packing of a 5-yard-long tube of 0.5 inch diameter presents the greatest problem which requires manual dexterity and patience.

One designation which will be noted in all gas chromatographic literature is *"number of plates of columns."* This is a somewhat meaningless expression, since there are no *"plates"* in the supporting phase. It is simply a term measuring the efficiency of the column corresponding to the Craig number for ideal stage, or originally in older columnar distillations. The higher the number, the better efficiency; for an ideal column it would be infinite; a common, satisfactory figure would be 4-5000.

The Stationary Phase

The stationary phase could be any liquid that is virtually non-volatile at operating column temperature. The choice of any particular liquid will depend upon the composition of the sample under analysis. The *basic* composition of the latter is usually surmised to some extent, *e.g.*, volatile oils; if absolutely unknown, trial and error procedure is the only solution. The liquid used must be non-sticky

and convenient to apply to the supporting phase. Usually, 15-50 W/W % is used and dissolved before packing in low-boiling solvent.

The liquid chosen must, of course, produce a differential partitioning which depends by and large on its solvent power for the vaporized components. If its absolute solvent power for a particular component is low, the latter will pass almost unhindered through the column, and its retention time will be short.

A certain "compatibility" must exist between the stationary phase and the components. A general rule is that the liquid and gas should show some chemical resemblance. Hence, one would choose, for instance, a non-polar stationary phase for the separation of paraffinic hydrocarbons.

Some solvents, however, have a wide range of applicability due to their composition. The phtalic acid esters, for instance, may be used for separating a wide variety of substances.

It is not difficult to find a suitable stationary phase at an operating temperature below 150°C. Practically all organic substances become too volatile above 200°C, and, beyond 250°, if the unknown is stable, only certain silicones, Apiezon grease, and bitumens are thermally stable. Of those liquids that may be used to advantage, are the following:

1. Phthalic acid esters with high Mw. alcohols; *e.g.*, 9-10 carbon atoms. These have low selectivity and, consequently, diversified application.

2. Mellitic acid esters (benzene hexacarboxylic acid).

3. Pure normal paraffins (C_{12} and higher), and mixtures of same (Solid Paraffin U. S. P.). These are excellent for separation of volatile hydrocarbons; *e.g.*, fuel gas. Temperature limit is 150°C.

4. Squalane (2, 6, 10, 15, 19, 23-hexamethyl tetracosane). As above, maximum operating temperature is 140°C.

5. Petroleum fractions (lubricating oils). Bitumen mixtures. Operating temperature—up to 300°C.

6. Silicones (phenyl-silicones) $(C_6H_5)_2 = Si = (C_6H_5)_2$ #703 and #550 (High vacuum grease has an extremely high temperature resistance).

7. Benzyldiphenyl with a temperature limit of 100°C.

8. Aromatic nitroesters such as dinitrodiphenic acid derivatives. Trinitrobenzoic acid ester with polyethylene glycol 400. These are specific for aromatics, but useless for paraffins. Maximum operating temperature is 120°C.

9. Polyglycols, *e.g.*, polyethyleneglycol 400. These are strongly *polar* liquids for analyses of oxygen and nitrogen containing compounds, poor for aliphatic hydrocarbons.

10. High boiling alcohols (C_{18}^{+}).

11. High molecular weight fatty acids. Maximum operating temperature is 140°C.

12. *Dimethyl formamide,* for hydrocarbon gases.

13. *Tricresylphosphate.* Conducive for chlorinated hydrocarbons. Maximum operating temperature is 125°C.

14. Diglycerol ($(CH_3OH\text{-}CH_2OH\text{-}CH_2)O_2$). Maximum operating temperature is 110°C. Excellent for the separation of isomeric alcohols.

15. Solutions of silver nitrate. Super-selective for resolution of overlapping olefins. Maximum operating temperature is 40°C.

As will be seen, we have a wide variety of liquid phases, some being of general application and some highly selective. Only imagination puts a limit to inventiveness; recently, *sugar solutions* have been reported to give great success in certain separations. It should be noted in some later example that there is no objection to using several of these in turn for the separation of chemically very heterogenous mixtures.

It is evident that this analytical tool will be most helpful in pharmacy for the analysis (qualitatively and quantitatively) of volatile oils.

Figures 2 and 3 demonstrate the appearance of a gas chromatogram of peppermint oils, prepared from 5 µl. of oil. Each peak represents one particular ingredient. The amplitude is non-significant depending only on the sensitivity setting. Note the reproducibility and small differences. The area of under each peak over the total areas represents the quantitative %-age fraction of each. The area may be measured with a planimeter or by making tangents to the

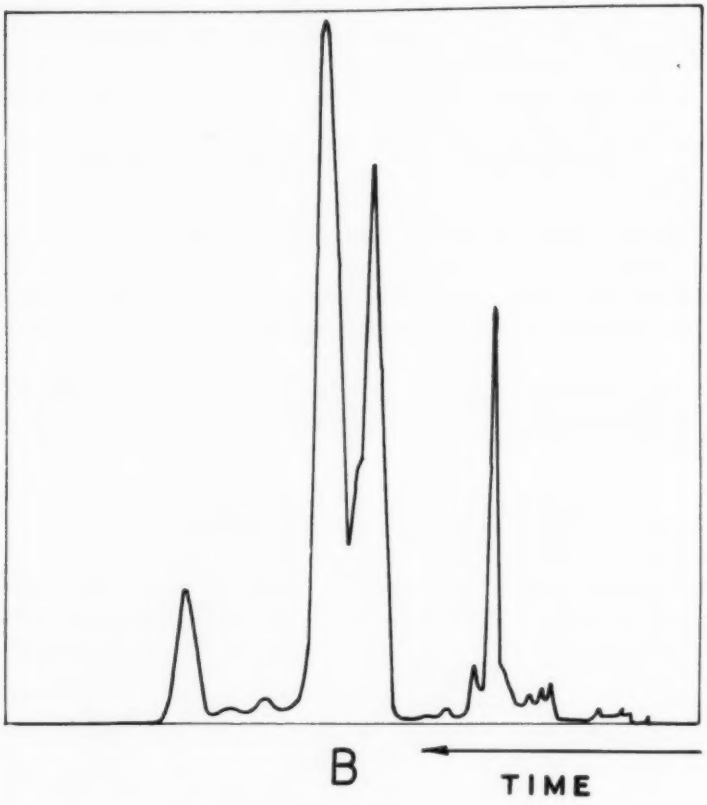

FIGURE 2

Gas chromatogram of Peppermint Oil, USP quality. Supporting phase: Firebrick; stationary phase: Squalane; gas: Helium; time: 52 min. (Orig.).

typical Gaussian curves (½ base line times height, etc.). Overlapping is treated by forming the closest triangles as above and measured in the conventional way. Admittedly, this procedure does not give great accuracy, but surpasses any other available method for determination of all components. Which ingredient each peak represents is unknown at present except that the highest peak represents menthol. More

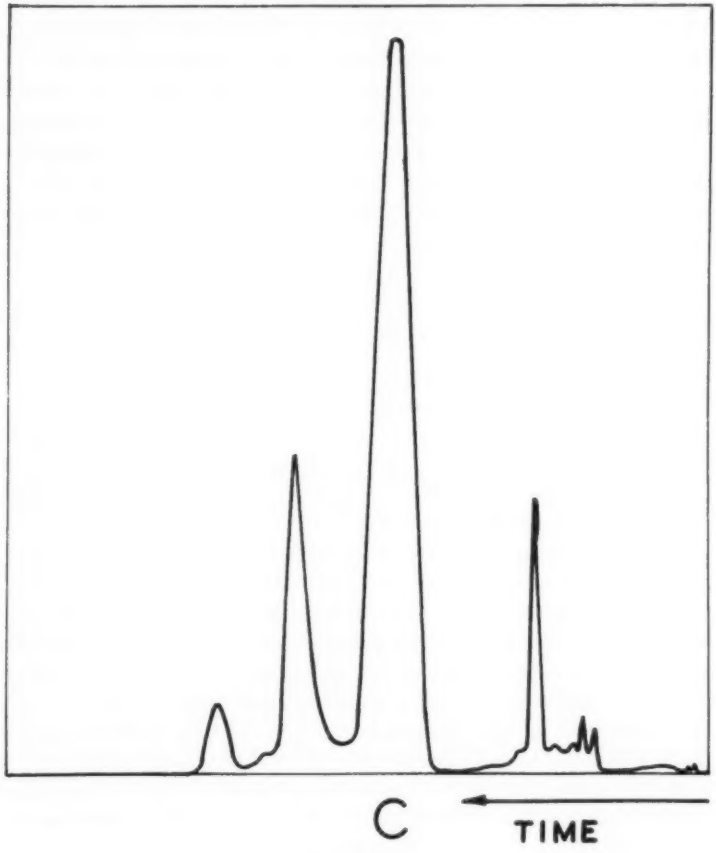

FIGURE 3

Gas chromatogram of Peppermint Oil, derived from plants, treated 5 times during their growth period with foliar sprays of gibberellic acid (50 ppm.). Same analytical set-up as Figure 2 (orig).

work will be needed to determine each component. The significant constant is the resolution time of each component and the retention time, which for any ingredient is a non-changeable characteristic under same temperature and pressure, comparable with the R_f-value in paper chromatography. Figs. 2 and 3 show clearly the potential of gas chromatography in comparative metabolic studies.

Liberti and Cartoni of the University of Messina presented a paper on GLC of volatile oils (mainly citrus oils) at the Gas Chromatography Symposium in Amsterdam in 1958 and concluded as follows:

"Gas chromatography is quite effective in achieving a complete investigation of most volatile oil components, with the exception of very high boiling compounds. Some precautions and limitations are noted: The stationary phase support may have a marked effect in promoting adsorption or catalytic decomposition of several compounds. Celite (100 mesh) is quite satisfactory provided it has been correctly inactivated. Firebrick is not as strongly recommended.

"Since several oxygen terpenes are heat sensitive, the operating temperature should be kept as low as possible.

"High efficiency columns must be used; 4-5000 theoretical plates are required for optimum results."

Of uses to which GLC has been put is the complete separation of fuel gas, radioactive gases (it is possible to collect the fractions as in a liquid-solid fraction collector, and the gas piped into a mass spectrometer or gas flow counter).

Gas chromatography also comes in handy for the analytical separation of lipids which has always presented problems by use of conventional methods. First, volatile methyl esters of the saponified fatty acid are prepared (micro quantities from biological tissues will suffice; *e.g.,* 1 cc. of blood). As methylating agent is used sodium methylate, and forty minutes are needed for complete analysis (1 mg. of each ester in solution gives beautiful separation). Diethyleneglycol succinate polyesters seems at present to be the most promising stationary phase for fat analyses. Naturally occurring, not too well-known resin acids may similarly prove a fertile field for pharmacognostical study.

Insecticide mixtures may according to a manufacturer's pamphlets be conveniently analyzed in microgram quantities on a silicone column at 250°C.

"Paraffin wax" and other high molecular hydrocarbons reportedly may be separated on the same column at 200° C.; C_{35} compounds have a retention time of 65 minutes.

Admittedly, the composition of volatile oils may vary strongly with their proveniences and ecological factors, but official standard oils do not vary significantly. However, GLC is an invaluable tool for biogenetic comparison studies and for study of the influence of external factors of any type.

Wilkins Instrument and Research Inc. of Walnut Creek, California claims that "sugars—as the methoxymethyl glycosides (sic!) are quantitatively determined on polyester columns. *Alpha* and *Beta* forms are easily separated."

For pharmacognosists, studies of volatile oils and other odoriferous vegetable substances is a wide open field and should prove a very fruitful area of research. There must be some 300 biological drugs which invite GLC study.

As examples of what this method may be used for are the composition of vanilla and strawberry flavors, bouquet of wine and other beverages. Smog is conveniently analyzed in less than 15 minutes giving results as parts per billion of ingredients in air. As if the above examples were not enough, the writer shall indicate some very recent developments.

Non-volatile compounds like proteins and amino acids may be determined, also. The method is based on, first, hydrolysis; next, methyl ester formation and vapor chromatography using silicone grease with 10% sodium caproate as a "tailing reducer" as stationary phase.

Two other reactions may be employed to attain volatile derivatives of amino acids. Ninhydrin oxidation will yield specified aldehydes; *e.g.*, formaldehyde from glycine, acetaldehyde from alanine, etc. This method reportedly gives quantitative results.[1] Decarboxylation of amino acids may be carried out by reacting mixtures with diphenylmethane or p-dimethylaminobenzaldehyde. In this case, glycine yields methylamine; alanine, ethylamine; ornithine, putrescine, etc. The yield of this method is quite variable and not satisfactory for quantitative work, and better oxidation catalysts are needed. The ninhydrin method gives quantitative results, but is not applicable to all amino acids. These same authors claim that the big advantage of

[1] Bier and Teitelbaum, *Ann. New York Acad. of Science, 72*, 641 (1959).

this method is its rapidity, and that no desalting of hydrolyzates is necessary.

As to GLC of pharmaceuticals, very few publications have been found. Eli Lilly and Company reports a new alcohol determination method after testing several official galenicals.[2] This method permits the ethanol assay to be carried out in less than half an hour as compared with at least one hour for the official distillation method. No pretreatment if I_2, NH_3 and other volatile substances are present is required in this procedure, the sample used only to be diluted with a known amount of acetone before being injected into the chromatograph. Results obtained by 2 analysts are very satisfactory and reproducible.

A promising work by J. Chr. Gjalbaek (School of Pharmacy, Universitets parken 2, Copenhagen) reports that six official pharmaceutical preparations were successfully analyzed by gas chromatography, using a Perkin Elmer fractometer model 154 B and a Speedomax recorder.[3] Helium was employed as the mobile phase. 0.007 ml. of aether spirituosus camphoratus Ph. Dan. IX was fractionated using diglycerol as liquid phase, column length 1 m.; a flow of 89 ml./min. of He and a temperature of 100°. Twenty-one per cent of Et_2O was obtained in less than 1 minute; 55 per cent EtOH, after 2 minutes; 15 per cent camphora, after 6; and 9 per cent H_2O, after 9 minutes. 0.007 ml. of Aqua Amygdalae Ph. Dan. was analyzed under the same conditions using a He flow of 48 ml./minute. After 2.5 minutes 3.4% EtOH was obtained; 0.4% PhCHO, after 8 minutes; and 96.2% of H_2O, after 12 minutes. Using silicone fluid DC 550 as liquid phase and a temperature of 150°, EtOH and H_2O were separated after 1 minute and ½% of menthol after 10 minutes from 0.008 ml. Spiritus mentholi Ph. Dan. 0.006 ml. Nitroglycerinum solutum concentrated and 0.0056 ml. Guttae nitroglycerini fortiores Ph. Dan. were analyzed at a flow of 102 ml. He/min. and a temperature of 200°. EtOH fractionated in less than 1 minute and $C_3H_5N_3O_9$ after 4 minutes. 0.007 ml. Aqua phenoli was analyzed at 104° and a gas flow of 137 ml./minute. H_2O was recovered after ½ minute and PhOH after 8.5 minutes. A mixture of 4 medicinal gases (0.25 ml.) was separated on silica gel at 30° and 52 ml. He in 1 minute. Thirty-one per

---

[2] *J. Amer. Pharm. Assoc., 49,* 320 (1960).

[3] *Dansk Tidsskr. Farm., 33* (9), 158-168 (1959).

cent O_2 separated in ½ minute, 24 per cent, N_2O in 2½; 22 per cent C_2H_2, in 5; and 24 per cent $(CH_2)_3$ cyclopropane in 13 minutes. Fuel gas on absorbent Molecular sieve 5A at 29° and 17 ml. He/minute rendered 45% H_2 in 1 minute; 2% O_2 in 2 minutes; 16% N_2 in 3 minutes; 14% CH_4 in 5 minutes; and 20% CO in 11 minutes.

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A NEW SUSPENDING AGENT FOR CALAMINE LOTION

By Joe E. Haberle * and William B. Swafford *

CALAMINE lotion was first introduced into the *National Formulary* in 1926 (1) and, since that time, it has been very popular for the treatment of many skin conditions (2). Even though this preparation is widely used, many efforts have been made to improve calamine lotion since it separates rapidly upon standing. The first official formula for this lotion contained no suspending agent (1), and its ingredients separated immediately after the product was prepared.

A suspending agent, bentonite magma, was added to the formula for the first time in 1942 (3) in an effort to reduce the rate of separation. This action did enhance the stability of calamine lotion, but its ingredients still settled out at a rate which made this preparation undesirable pharmaceutically. Another attempt to increase the stability of calamine lotion was made in 1950 when a combination of polyethylene glycol 400 and polyethylene glycol 400 monostearate replaced the bentonite magma in the official formula (4). Although this modification resulted in an improvement with respect to retarding separation, new difficulties were encountered. The USP XIV formula would not pour freely from small bottles, was incompatible with phenol, and foamed excessively during manufacture (5).

With these disadvantages of the new formula apparent, investigators again centered their attention on the task of producing a new calamine lotion which would meet the requirements of a good pharmaceutical suspension. Marcus and DeKay produced a lotion containing 2% sodium alginate as the suspending agent which exceeded the official product in stability (6). Zopf and others found that increasing the polyethylene glycol 400 monostearate in the USP XIV formula from 2% to 4% prevents loss of suspending power when phenol is added (7). Goldstein presented a formula containing sodium carboxymethylcellulose and Aerosol OT which pours easily, does not foam excessively when shaken, and is compatible with

* Assistant Professor, College of Pharmacy, University of Tennessee, Memphis 3, Tennessee.

phenol (8). Veegum has also been suggested as a suspending agent for calamine lotion (9) and (10). However, none of these modifications in the calamine lotion formula proved sufficiently popular as bentonite magma again became the suspending agent for the official product in the USP XV (11), and is presently still serving in that capacity.

The object of this project was to investigate the suspending properties of Cellosize WP-4400 * in calamine lotion and to compare the physical properties of formulations containing this material with the official preparations, both plain and phenolated. Cellosize WP-4400 is a non-ionic synthetic colloid possessing high thickening power and is soluble in hot or cold aqueous solutions (12).

Experimental

A number of modified calamine lotion formulations were manufactured in which Cellosize WP-4400 replaced bentonite magma as the suspending agent. The concentration of this non-ionic material was varied from ¼ per cent to 2 per cent.

Each lotion was prepared in the same manner. The Cellosize WP-4400 was thoroughly mixed with 8 Gm. of calamine and 8 Gm. of zinc oxide in a mortar, and enough calcium hydroxide solution was added in divided portions, triturating after each addition, to make 100 ml. One per cent phenolated lotions were also made and evaluated.

Fifty milliliters of each lotion were stored in a 50 ml. cylindrical graduate and sealed with plastic so that separation rates could be determined, and the remaining portion of each formulation was stored in two-ounce prescription bottles to evaluate pourability. Calamine Lotion USP XVI and Phenolated Calamine Lotion USP XVI were manufactured and used as standards.

The separation rates and pourability evaluations are shown in the table given. The amount of settling was recorded the same day of manufacture and then weekly thereafter for a period of six weeks. The observation was made the first day since the official preparations are known to settle out very rapidly. The ability of each sample to flow freely from a two-ounce prescription bottle was determined immediately after preparation and at the end of 43 days.

* Cellosize WP-4400 is a trade name for hydroxyethyl cellulose produced by Union Carbide Chemicals Co., Division of Union Carbide Corporation, New York, N. Y.

CALAMINE LOTION FORMULATIONS CONTAINING CELLOSIZE WP-4400[1]

Formulation	*Per Cent Suspending Agent*	*Percentage Separation*							*Pourability*	
		1 Day	8 Days	15 Days	22 Days	29 Days	36 Days	43 Days	1 Day	43 Days
Calamine Lotion U. S. P. XVI		50	55	56	56	56	56	56	Good	Good
Phenolated Calamine Lotion U. S. P. XVI		37	37	37	38	38	39	39	Good	Good
Lotion #1	¼	2	26	*	*	*	*	*	Good	Good
Phenolated Lotion #1	¼	2	16	*	*	*	*	*	Good	Good
Lotion #2	½	2	16	*	*	*	*	*	Good	Good
Phenolated Lotion #2	½	1	4	6	8	8	12	16	Good	Good
Lotion #3	¾	0	4	8	12	16	20	22	Good	Good
Phenolated Lotion #3	¾	0	2	3	3	3	3	3	Good	Good
Lotion #4	1	0	2	7	8	12	16	17	Good	Good
Phenolated Lotion #4	1	0	0	1	2	2	2	2	Good	Good
Lotion #5	1¼	0	2	4	6	8	11	12	Good	Good
Phenolated Lotion #5	1¼	0	0	1	1	1	2	2	Good	Good
Lotion #6	1½	0	2	3	4	6	9	10	Fair	Fair
Phenolated Lotion #6	1½	0	0	1	1	1	2	2	Fair	Fair
Lotion #7	1¾	0	1	2	3	4	6	6	Poor	Poor
Phenolated Lotion #7	1¾	0	0	0	0	0	0	0	Poor	Poor
Lotion #8	2	0	1	2	2	3	4	4	Poor	Poor
Phenolated Lotion #8	2	0	0	0	0	0	0	0	Poor	Poor

[1] Cellosize WP-4400 is a trade name for hydroxyethyl cellulose produced by Union Carbide Chemicals Co., Divisions of Union Carbide Corporation, New York, N. Y.

* Per cent separation impossible to determine due to extreme cloudiness.

Calamine Lotion USP XVI and Phenolated Calamine Lotion USP XVI separated 50 per cent and 37 per cent respectively the first day while none of the formulations containing Cellosize WP-4400 settled more than 2 per cent. Lotion #1, phenolated lotion #1, and lotion #2 became extremely cloudy after the first eight days which made it impossible to observe separation rates on these formulations.

The percentage separation of the active ingredients decreased as the concentration of Cellosize WP-4400 was increased, and it was also noticed that the phenolated lotions settled out less rapidly than the plain lotions containing the same amount of this suspending agent.

All the formulations studied containing less than 1½% suspending agent poured readily from two-ounce prescription bottles on the day of manufacture and at the end of the study. However, those preparations containing 1½% to 2% Cellosize WP-4400 were much thicker and were difficult to pour from the small containers in which they were stored.

All the modified calamine lotions studied were found to have good spreading properties and, when they were applied, the resulting films would not rub off on the clothes.

Lotion #5 and phenolated lotion #5 were chosen as the best formulations which were evaluated. Lotion #5 separated only 12 per cent in 43 days while the official calamine lotion separated 56 per cent, and phenolated lotion #5 settled but 2 per cent compared to 39 per cent for the official phenolated preparation. Both of these modified calamine lotions can be easily poured from small prescription bottles, have good spreadability, and dry to a nontransferable film when applied to the skin. In addition, these lotions can be prepared extemporaneously in small quantities with equipment found in the average prescription department. The formulas for these two lotions are presented below.

Lotion #5			*Phenolated Lotion #5*		
Calamine	8	Gm.	Calamine	8	Gm.
Zinc Oxide	8	Gm.	Zinc Oxide	8	Gm.
Cellosize WP-4400	1¼	Gm.	Cellosize WP-4400	1¼	Gm.
Calcium Hydroxide Solution q.s. ad	100	ml.	Liquefied Phenol	1	ml.
			Calcium Hydroxide Solution q.s. ad	100	ml.

Summary and Conclusions

A synthetic colloid, Cellosize WP-4400, has been evaluated as a suspending agent for calamine lotion. A modified lotion containing this material has been formulated which has a much slower separation rate than Calamine Lotion USP XVI. This formulation is compatible with phenol and pours easily from small prescription bottles. It also has good spreading properties, forming a nontransferable film upon application to the skin. The preparation of this lotion is simple and can be accomplished with equipment routinely found in a prescription department.

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THE PREPARATION AND EVALUATION OF GRAPEFRUIT PEEL TINCTURE AND GRAPEFRUIT SYRUP *

By N. H. Franke † and J. L. Burge ††

A grapefruit peel tincture was prepared by maceration of the grated outer yellow peel of the fresh fruit. The determination of the oil content of the tinctures was done by an adaption of the A. O. A. C. precipitation method. A grapefruit syrup was prepared from the tincture, using heavy magnesium oxide as the filtering agent. Organoleptic tests indicated that grapefruit syrup compared favorably in taste preference with five other vehicles which had ranked high in taste preference tests conducted by other workers. Grapefruit syrup also appeared to have a high value in disguising the salty taste of ammonium chloride and a mediocre value in disguising the bitter taste of quinine hydrochloride.

THE grapefruit, *Citrus Paradisi*, Macf. (*C. Maxima* var. *uvacarpa*, Merr. & Lee), or pomelo, is grown in good quantity in the United States, but of unknown origin (I). It is thought to have originated in the West Indies, but no one seems to know when the grapefruit was so-called. It is thought to be a hybrid of the pummelo and the sweet orange. Recent production has reached over 60,000,000 boxes a year; therefore, it may be considered to be readily available and in relatively good constant supply.

Grapefruit oil is recovered commercially by expression and by distillation. In 1947, over 33,000 pounds of the expressed oil had been produced. It should be noted that the oil glands are located deeply in the peel. The peel can be easily grated, as in the case of the lemon or orange. Analysis of the cold-pressed oil varies within the following limits: sp. gr. 25°/25°, 0.8532 to 0.8508; optical rotation at 25°, + 92.96° to + 91.19°; refractive index at 20°, 1.4761 to 1.4746; aldehyde content calculated as decyl aldehyde, 1.67% to

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1.49%; and ester content, 4.20% to 2.11%. The main constituent is limonene (about 90%). Also isolated from the oil were octyl aldehyde, decyl aldehyde, cirtal; acetic acid, octylic acid, decylic acid, probably as esters; n-octyl alcohol, n-octyl acetate, n-nonyl alcohol, geraniol, geranyl acetate, methyl anthranilate, and d-cadinene (2).

Experimental

Preparation of Grapefruit Peel Tincture.—Three samples of grapefruit tincture were prepared by the method for making Sweet Orange Peel Tincture, U. S. P. XV(3). Only the maceration period was changed so that Tincture No. 1 was macerated for three days, No. 2 for six days, and No. 3 for nine days.

After filtering, all tinctures had a deep golden-yellow color and an odor characteristic of the citrus fruits.

In order to ascertain the optimum length of maceration time, the oil content of each of the sample tinctures was determined. For this purpose, the precipitation method (4), official in *Official and Tentative Methods of Analysis* of the Association of Official Agricultural Chemists, as modified by Sheffield and Thompson (5) was used. The results of the determination of the solubility correction factor for grapefruit oil * are shown in Table I. These results indicate that this method of assay is satisfactory for grapefruit peel tincture.

The results of the assay of grapefruit peel tincture, as shown in Table II, indicate that the U. S. P. XV method of preparation was adequate to provide a satisfactory tincture, and that additional maceration time did not appreciably change the oil content.

Preparation of Grapefruit Syrup.—Three different samples of grapefruit syrup were prepared by the method given in U. S. P. XV (6). The only change was in the amount of tincture used. Syrup A contained 100 ml.; Syrup B, 50 ml.; and Syrup C, 10 ml. of grapefruit peel tincture. Syrup A had a light yellow color and a strong flavor, but left a bitter, disagreeable aftertaste. Syrup B was a very pale yellow and of pleasant odor and taste. Syrup C was nearly colorless and of faint, delicate flavor. Therefore, Syrup B was selected.

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* Expressed grapefruit oil was furnished by Fritzsche Brothers, Inc., 76 Ninth Ave., N. Y. 11, N. Y.

Following the method of Sheffield and Thompson (5), various filtering media were tested for efficacy in clarifying the syrup of grapefruit. The results, shown in Table III, indicate that heavy magnesium oxide was the most efficacious of those media tested. Although talc showed no appreciable reaction with the syrup containing the acid, the removal of the color makes it undesirable. The reaction of the heavy magnesium oxide with the acid containing syrup and the need for a sharp, tangy taste which would enhance the flavor quality of the finished product suggest the addition of the acid after clarification.

TABLE I

DETERMINATION OF CORRECTION FACTORS FOR GRAPEFRUIT OIL IN ASSAY OF GRAPEFRUIT PEEL TINCTURE.

Known Per Cent of Oil	*Determined Per Cent of Oil by Precipitation*	*Solubility Correction Factor*
5.0	4.8	0.2
4.5	4.3	0.2
4.0	3.8	0.2
3.5	3.3	0.2
3.0	2.8	0.2
2.5	2.3	0.2
2.0	1.8	0.2
1.5	1.3	0.2
1.0	1.4	0.2
0.5	0.45	0.05

TABLE II

ASSAY OF GRAPEFRUIT PEEL TINCTURES FOR OIL CONTENT.

Marceration Time in Days	*Per Cent Oil*
3	1.60
6	1.70
9	1.30

In an effort to get some indication of the degree of deterioration of the syrup and the tincture, three samples of both the tincture and syrup were packaged in clear glass under hermetic seal and exposed to sunlight for one month and then kept at room temperature in the dark for eleven months. There was no indication of any change in color, odor, or taste. Six samples of the syrup were packaged in clear glass and half kept at room temperature in a dark place, the remainder kept in the light. This was repeated with the syrup containing 0.1% benzoic acid. In neither case at the end of one year was there any indication of a change in odor, color, or taste. After four years, a container of the tincture which had been stored at room temperature in a dark place was examined and found to have darkened in color slightly, produced a very light sediment, and acquired a slight terebinthinate odor and taste.

TABLE III

THE EFFICIENCY OF FILTERING AGENTS IN THE PREPARATION OF GRAPEFRUIT SYRUP

Filtering Agent	*Amount of Filtering Agent Gm.*	*Filtration Time, Min.*	*Color*	*pH of Solution Filtered With Citric Acid*	*pH of Solution (Citric Acid Added After Filtration)*	*pH of Final Syrup*
Calcium Carbonate [a]	2.5	18	Pale	6.80	2.22	2.22
Magnesium Oxide [b] (Heavy)	2.5	10	Rich	10.25	3.4	3.50
Magnesium Oxide [c] (Light)	2.5	13	Medium	10.50	2.90	2.97
Talc [d]	2.5	15	Very Pale	4.10	3.80	3.80

[a] 10 ml. portion returned once.
[b] 10 ml. portion returned twice.
[c] Filtrate clear immediately.
[d] Did not clear.

Organoleptic Tests.—In order to evaluate grapefruit syrup in terms of palatability alone, organoleptic tests were conducted in which the flavor preference of grapefruit syrup and five other flavoring syrups was determined. The tests were conducted in the same manner as that developed by Wright (7). Thirty-two subjects participated in each test, and ninety-six subjects took part in all the tests. To avoid the persistance of flavors, all vehicular solutions contained 10% by volume of the syrup in distilled water. The results were expressed as a percentage of a perfect first choice, and the average per cent score for each syrup is shown in Table IV. This Table shows that grapefruit syrup compares favorably with the six most preferred syrups as rated by Wright (7) and by Sheffield and Thompson (5). Syrup of Citric Acid was used in place of the tangerine syrup used by Sheffield and Thompson (5) in order to compare so widely used an official vehicle with grapefruit syrup, also a citrus type fruit. It is noted that Citric Acid Syrup rated low here as it did in Wright's evaluation (7).

The value of grapefruit syrup as a disguising agent for drugs was determined by duplicating the procedure of Purdum (8). The threshold taste for the drug in an aqueous solution was compared with the threshold taste for the drug in a solution of the vehicle. The difference between the two thresholds is expressed numerically

TABLE IV

TASTE PREFERENCE OF SEVEN SYRUPS.

Vehicle	*Mean Per Cent Preference*
Cacao Syrup (N. F. VIII)	77
Cherry Syrup (N. F. VIII)	69
Grapefruit Syrup	68
Raspberry Syrup *	67
Orange Syrup (U. S. P. XIII)	63
Cinnamon Syrup (N. F. VII)	59
Citric Acid Syrup (U. S. P. XV)	46

* Prepared from an artificial product.

as the disguising potential of the vehicle for the drug used. Generally, the higher the mean disguising potential, the greater the disguising value for the drug used. The concentrations of ammonium chloride and quinine hydrochloride representing salty and bitter drugs respectively were used according to the procedure of Sheffield and Thompson (5). The results are recorded in Tables V and VI. From Table V, it can be seen that grapefruit syrup ranks favorably with the first six vehicles in its ability to mask the salty taste of ammonium chloride. However, in Table VI, it will be seen that grapefruit syrup has a mediocre value in disguising the bitter taste of quinine hydrochloride although it is preferable to at least 13 other vehicles.

Conclusions

(1) The official method for the preparation of Sweet Orange Peel Tincture is a satisfactory method for the preparation of grapefruit peel tincture.

(2) The precipitation method, adapted for the assay of grapefruit peel tincture for its oil, is a satisfactory method.

TABLE V

AMMONIUM CHLORIDE DISGUISING EFFICACY OF GRAPEFRUIT SYRUP[a]

Vehicle	*Mean Threshold in Water ± Standard Error* $m_2 \pm \varepsilon_2$	*Mean Threshold in Vehicle ± Standard Error* $m_1 \pm \varepsilon_1$	*Mean Disguising Potential ± Standard Error* $D \pm \varepsilon$	*Significance of Difference* $\frac{m_1 - m_2}{\sqrt{\varepsilon_1^2 + \varepsilon_2^2}}$
Grapefruit Syrup	2.20 ± 0.13	4.56 ± 0.18	2.36 ± 0.25	10.28
Tangerine Syrup	3.33 ± 0.17	5.56 ± 0.18	2.23 ± 0.12	9.02
Glycyrrhiza Syrup	3.56 ± 0.22	5.72 ± 0.29	2.16 ± 0.24	5.97
17 Vehicles in Order of Decreasing Mean Disguising Potentials[b]	—	—	—	—
Syrup (simple)	4.15 ± 0.26	5.15 ± 0.23	1.00 ± 0.17	2.92

[a] Table reproduced from Sheffield and Thompson (5) with the addition of the values for grapefruit syrup.

[b] Syrup of raspberry; orange flowers; citric acid; tolu balsam; acacia; orange; aromatic eriodictyon; cherry; cocoa, N. F. V; prepared cacao, N. F. VI; thyme; wild cherry; cinnamon; althea; elixir of glycyrrhiza; compound syrup of sarsaparilla; and aromatic elixir.

(3) A satisfactory method for the preparation of grapefruit syrup has been devised.

(4) Tests with four different filtering media indicate that heavy magnesium oxide is satisfactory, if the citric acid is added after filtration.

(5) Organoleptic tests conducted with grapefruit syrup indicate that it compares favorably in taste preference with five vehicles which ranked high in taste preference tests conducted by other workers, and was far superior to Citric Acid Syrup, an official product now in good usage.

(6) It has been shown that grapefruit syrup has a high value for disguising the salty taste of ammonium chloride and a mediocre value for disguising the bitter taste of quinine hydrochloride.

Acknowledgment

The authors wish to express their appreciation to H. M. Hutchinson, J. H. Hayes, and B. B. Hunt for the kind assistance rendered by them.

TABLE VI

QUININE HYDROCHLORIDE DISGUISING EFFICACY OF GRAPEFRUIT SYRUP[a]

Vehicle	*Mean Threshold in Water ± Standard Error* $m_2 \pm \varepsilon_2$	*Mean Threshold in Vehicle ± Standard Error* $m_1 \pm \varepsilon_1$	*Mean Disguising Potential ± Standard Error* $D \pm \varepsilon$	Significance of Difference $\frac{m_1 - m_2}{\sqrt{\varepsilon_1^2 + \varepsilon_2^2}}$
Prepared Cacao Syrup (N. F. VI)	3.50 ± 0.31	8.17 ± 0.40	4.67 ± 0.26	9.18
4 Vehicles[b]	—	—	—	—
Tangerine Syrup	2.70 ± 0.13	6.13 ± 0.13	3.43 ± 0.16	19.05
Grapefruit Syrup	3.03 ± 0.09	6.44 ± 0.13	3.41 ± 0.18	21.58
Glycyrrhiza Elixir	3.73 ± 0.25	6.93 ± 0.42	3.20 ± 0.34	6.52
14 Vehicles[c]	—	—	—	—
Aromatic Elixir	3.38 ± 0.25	4.97 ± 0.32	1.59 ± 0.17	3.88

[a] Table reproduced from Sheffield and Thompson (5) with the addition of the values for grapefruit syrup.

[b] Syrup of glycyrrhiza, cocoa, N. F. V; aromatic eriodictyon; and thyme syrup.

[c] Syrup of tolu balsam, compound sarsaparilla, raspberry, cherry, cinnamon, citric acid, althea, wild cherry, simple, acacia, orange flowers, simple orange.

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SELECTED ABSTRACTS

Iron Therapy in Chronically Fatigued, Nonanemic Women. Beutler, E., Larsh, S. E., and Gurney, C. W. *Ann. Internal Med. 52:*378 (1960). A double-blind study of the effects of iron therapy in chronically fatigued but healthy women having hemoglobin levels above 12 Gm. % was undertaken by the authors. Some of the women also had symptoms of headache, dizziness, and nervousness.

The women were divided into 5 groups according to the degree of iron depletion, based upon the results of plasma iron and iron-binding capacity determinations. Either 0.3 Gm. ferrous sulfate or a placebo (0.3 Gm. bismuth subcarbonate) was administered over a period of about 3 months. No drug was then given for about 1 month and then the other drug was given for 3 months. A total of thirty women completed the study.

In the patients with the most severe degrees of iron depletion, the average hemoglobin of the blood rose significantly when iron was given but not when the placebo was administered. Neither iron nor placebo produced significant hemoglobin changes in patients with greater than trace amounts of iron in the bone marrow. Some symptomatic improvement was experienced by all but 2 patients.

The authors concluded that this study proved that the administration of iron to women with depleted bone marrow iron stores, and with hemoglobin values above 12 Gm.%, caused a rise in hemoglobin. They stated that the study also suggested that iron therapy will exert a beneficial effect upon the chronic fatigue, headaches, paresthesias, and dyspnea from which nonanemic, otherwise healthy women frequently suffer.

A Study of the Stability of Aspirin in Solution. Bolton, S. *Drug Standards 28:*117 (1960). The rate of decomposition of aspirin in solution was studied at a constant temperature of 30°C. The pH was varied from 3.92 to 6.37 and additives included citrates, phosphates, acetates, and sodium hydroxide.

The citrates have long been employed as solubilizers for aspirin. However, it has been shown previously that aspirin is not stabilized in solution in the presence of citrate.

The author used recrystallized acetylsalicylic acid in a concentration of 0.055 molar in most cases. In one series, a concentration of 0.0055 molar and, in another, 0.222 molar was used. Sodium citrate, potassium citrate, sodium acetate, and sodium phosphate were used at varying concentrations from as low as 0.0017 molar to as high as 1.35 molar. The pH was adjusted by the addition of sodium hydroxide.

The rate of hydrolysis of aspirin was found to be essentially independent of the nature and concentration of the additive at a given pH. In one instance in which sodium citrate and sodium phosphate were used in combination at a pH of 5.9, the half life was slightly less than in the presence of either salt alone. The rate of hydrolysis was related to the pH, however. At a pH of 3.92, the half life was 42 hours. The half life decreased steadily to 35 hours at a pH of 5.4 and 33¼ hours at a pH of 6.37. The concentration of aspirin appeared to have no significant effect upon the rate of hydrolysis, for a 0.0055 molar solution had a half life of 35 hours at a pH of 5.4 and a 0.222 molar solution had a half life of 35½ hours at the same pH.

BOOK NOTICES AND REVIEWS

A Pictorial Vade-Mecum for General Zoology. Francis M. White. iii + 137 pp. Illus., 3-hole punch. Burgess Publishing Co., Minneapolis, Minn., 1960. Price: $4.25.

One of the noteworthy characteristics of members of the teaching profession is their constant attempts to improve the methods used in presenting a course of study. College laboratory courses in the biological sciences, by their very nature and purpose, lend themselves to changes for improvement in the ways of disseminating information and arousing enthusiasm for the subject in the students. In the process of seeking a means to this end, many instructors create their own laboratory manuals and add to and subtract from them as time and experience indicate it to be wise and necessary. Oftentimes, after a period of testing and evaluation on "home ground," a particular "edition" appears to be worthy of formal publication and distribution on a wider scale and is then offered to other institutions for adoption. Professor White's *Vade-Mecum* is such a laboratory manual.

This is a unique laboratory book for a course in general zoology. It contains, *inter alia*, 96 photographs, 113 drawings strictly outlining organisms or particular structures, and space for additional drawing assignments, but it is almost devoid of directions or instructional material. It is the intent of the author to provide the student in the laboratory with merely a framework in which *he, the student,* is to record *his* observations, leaving the course textbook (such as Hegner and Stiles' *College Zoology*) as the source of detailed information. This approach has proved to be successful at the Philadelphia College of Pharmacy and Science (where the author is Associate Professor of Zoology) after having used there for a number of years mimeographed or printed detailed laboratory instructions in addition to a standard textbook. It would appear that this "new" approach could be used advantageously by other institutions.

The *Pictorial Vade-Mecum* is designed for a six-hours a week course spanning a full academic year. It provides a broad coverage of the animal kingdom and includes those organisms in general use. It must be noted, with regret, that *Ascaris lumbricoides*, as in the case

of so many introductory courses in zoology, is used as the "type" nematode. Admittedly, the size of this species has made it a useful and desirable laboratory tool. However, it is this reviewer's opinion that the free-living nematodes, albeit requiring a microscope for study, are more representative of the group. In view of their transparency and the fact that they are so readily available in the living state, they would prove to be more interesting and stimulating than the usually embalmed ascarids.

The outline drawings deal with 17 invertebrates and 10 chordates. Each outline is clearly printed and has ample space for recording observations. Where useful, special space is provided for writing in taxonomic information. The individual sheets are punched so that, if desired, they can be removed from the spiral wire binding, submitted for correction and evaluation by the instructor, and then kept in a standard $8\frac{1}{2}'' \times 11''$ three-ring binder. The fact that the drawings can be kept in the original binding along with the photographs, or can be readily placed in another binder with other information, is a desirable feature.

The photographs appear to have been chosen with thought and have been arranged in the manual with purpose. They supplement assigned material and drawings, rather than replace them. Most are remarkably well-reproduced and add greatly to complete the overall coverage of animal biology. The photographs are not labelled but space is provided for the student to do this if so desired. Unlabelled, the photographs may serve as a convenient means of testing or review. The photographs are derived from different sources and acknowledgments are clearly indicated.

In addition to presenting a variety of zoological specimens from the taxonomic and comparative anatomical viewpoint, drawing space and photographs for special subjects, such as embryology, which are usually included in a basic course in general zoology, are also provided. An experiment on the effect of digitalis, ethyl alcohol, and cascara upon *Daphnia* is included and tables for recording results are provided. While this experiment may be of particular interest to majors in pharmacy, it should fascinate all first year students since it employs *living* biological specimens, and nothing holds the interest of students in biology as live organisms.

The offset printing work is very well done. There are, unfortunately, a few typographical errors and inversions of photographs;

however, these should not be too troublesome and they will be corrected in subsequent editions.

An outline of the course in general zoology as presented at the Philadelphia College of Pharmacy and Science is offered for consideration as a guide. This program obviously can be modified according to the desires of the instructor and his particular institution. The *Vade-Mecum* itself appears to be flexible enough to be adaptable to a variety of approaches to the teaching of general zoology; it is a laboratory manual which could be of benefit to both instructors and students.

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Advanced Organic Chemistry, 3rd Edition. By G. W. Wheland. xi + 871 pp. John Wiley & Sons, Inc., 440 Fourth Avenue, New York 16, N. Y., 1960. Price: $17.50.

The new edition of Professor Wheland's well-known work encompasses much of the new material relating to physical organic chemistry which has come to the fore in the intervening eleven years since the publication of the second edition.

Many chapters; e.g., Molecular Rearrangements, Tautomerism and Electrostatic Effects in Organic Chemistry, have been expanded. The chapter on Addition Compounds now discusses inclusion, charge-transfer, and "sandwich" compounds. Practically all of the material has been rearranged somewhat.

The author states that some material has been deleted to allow for inclusion of new material, but this has been accomplished judiciously, since nothing of importance to the over-all appreciation of the text appears to be missing.

It is unfortunate that the price of so many books, deemed almost a necessity by the chemist—student, teacher, and practitioner—is becoming somewhat prohibitive, but this book is fully recommended for the library of any organic chemist desirous of more than a mere "pot-boiling" knowledge of his science.

A. R. GENNARO

Biochemistry of Plants and Animals, An Introduction. M. Frank Mallette, Paul M. Althouse, and Carl O. Clagett. xiii + 552 pp. John Wiley & Sons, Inc., New York and London, 1960. Price: $8.50.

Although this book is essentially new, it originated from *Introduction to Agricultural Biochemistry*, by Dutchen, Jensen, and Althouse, published in 1951. It is divided into three major sections devoted to general biochemistry, plant biochemistry, and animal biochemistry. This book is intended to provide a general knowledge of biochemistry for students in the agricultural sciences; however, an effort has been made to orient the treatment broadly enough for elementary courses for students from other disciplines.

Staining Procedures. Second Edition, revised by H. C. Conn, Mary A. Darrow, and Victor M. Emmel. xii + 289 pp. The Williams and Wilkins Company, Baltimore, 1960. Price: $5.00.

This publication, sponsored by the Biological Stain Commission, represents a complete revision of the loose-leaf form of the first edition, published periodically during the period from 1943 to 1955. The procedures given are not intended to be considered *standard* or *official* but represent methods used in microtechnique in the laboratories of the Commission members. The material is presented in a standardized form for the convenience of users and divided into three major divisions of staining procedures: animal histology, plant histology, and microbiology. An excellent bibliography is included.

Orientation to Pharmacy. Edited by Henry M. Burlage. x + 306 pp. McGraw-Hill Book Company, Inc., New York, 1959. Price: $6.95.

This book is based upon the papers and discussions presented at the Teachers' Seminar in Pharmacy held at Butler University in August 1956. The book is intended to introduce the student of pharmacy to the professional subjects he will meet in his academic program.

Dictionary of Atomic Terminology. Edited by Lore Lettenmeyer. 298 pp. Philosophical Library, New York, N. Y., 1959. Price: $6.00.

This dictionary attempts to provide a selection of the essential scientific and technical terms employed in connection with atomic and nuclear physics, reactor engineering, radiation physics, and associated fields, with the object of facilitating the study of the relevant foreign literature on the subject; namely, German, French, and Italian.

Workbook of Solutions and Dosage of Drugs (Including Arithmetic), Sixth Edition. Ellen M. Anderson. 176 pp. C. V. Mosby Company, St. Louis, Missouri, 1960. Price: $3.25.

The purpose of this workbook is to provide a quick basic review in arithmetic, methods of preparing dosages of drugs and solutions and teaching aids so that the student in nursing will acquire those special tools that are a part of the total knowledge necessary to give effective nursing care. An answer book is included for use with the workbook.

Organic Reactions. Volume XI. Arthur C. Cope, Editor-in-Chief. vii + 501 pp. John Wiley & Sons, Inc., New York, N. Y., 1960. Price: $12.00.

Since its inception in 1942, *Organic Reactions* has become one of the standard reference works in organic chemistry. This new volume, in the same format as its predecessors, fully documents five familiar reactions: The Beckmann Rearrangement, The Demjanov and Tiffeneau-Demjanov Ring Expansions, Arylation of Unsaturated Compounds by Diazonium Salts, The Favorskii Rearrangement of Haloketones, and The Production of Olefins from Amines by the Hoffmann Elimination and Amine Oxide Pyrolysis. A subject index for this volume and a cumulative author and chapter index for all eleven volumes completes the book.

It is unnecessary to relate to any organic chemist the value of possessing this annal of chemistry.

A. R. GENNARO

Quantitative Pharmaceutical Chemistry, Fifth Edition. Glenn L. Jenkins, John Christian, and George P. Hager. xviii + 552 pp. McGraw-Hill Book Company, Inc., 1957. Price: $8.50.

This text is a thorough revision of the fourth edition, with new chapters on radioactivity and chromatography added. New illustrations and much new material pertinent to instrumental methods have been introduced. Part one is devoted to gravimetric and volumetric analysis, and parts two and three contain special methods of pharmaceutical analysis and physiochemical methods. Useful references to other textbooks and treatises on general and special methods of analytical procedure have been revised and extended.

Poisoning, A Guide to Clinical Diagnosis and Treatment. Second Edition. W. F. vonOettingen. xii + 627 pp. W. B. Saunders Company, Philadelphia, Pa., 1958. Price: $8.75.

This edition presents new types of poisoning, new methods for detection of toxic materials in biological specimens, and new procedures for the treatment of poisonings. More than half of the text is devoted to a discussion of the symptoms and treatments of various types of poisoning and of toxic reactions of drugs.

Husa's Pharmaceutical Dispensing, Fifth Edition. Edited by Eric W. Martin. 729 pp. Mack Publishing Company, Easton, Pa., 1959. Price: $12.00.

This book is a completely revised edition of the *Textbook of Pharmaceutical Dispensing* by William J. Husa, first published in 1931. The latest information on modern methods of compounding drug products—physical, chemical, and therapeutic incompatabilities—is presented in a clear, concise manner. The book contains examples of new prescriptions reproduced to illustrate various points. The text is extensively illustrated and has a comprehensive index.

The Lynn Index, A Bibliography of Phytochemistry. Organized and edited by John W. Schermerhorn and Maynard W. Quimby. 69 pp. Massachusetts College of Pharmacy, Boston, 1960.

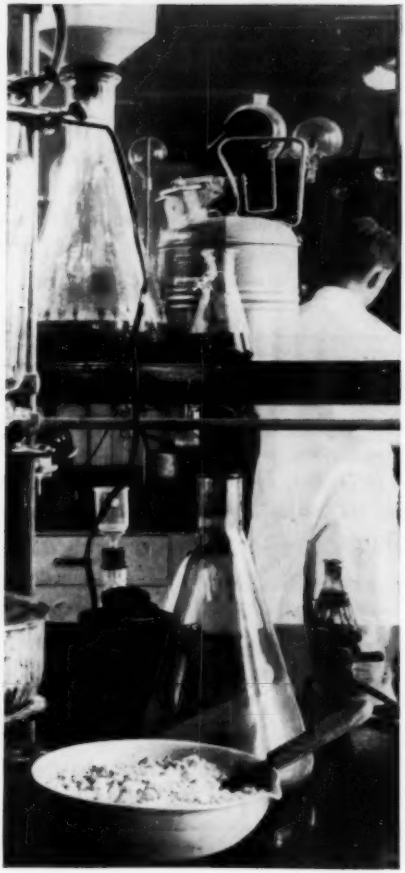
Monograph IV of the Lynn Index is devoted to the Order, *Glumiflorae,* including the Families, *Cyperaceae* and *Gramineae.*

Requirements for Biological Substances. 5. Requirements for Smallpox Vaccine. Report of a Study Group. World Health Organization Technical Report Series No. 180. 24 pp. WHO, Geneva, 1959. Price: $0.30.

This report represents the collective views of an international group of experts on recommendations for the requirements which should be fulfilled by a preparation of smallpox vaccine in order to ensure that the product is a safe, reliable, and potent prophylactic agent.

Essential Oils and Aromatic Chemicals, A Symposium held at Dehra Dun, October 6-9, 1955, under joint auspices of Council of Scientific and Industrial Research and the Forest Research Institute and Colleges, New Delhi, India. xx + 174 pp. Printed by S. N. Guha Ray at Sree Saraswaty Press Ltd., Calcutta, India, 1958.

A number of original papers dealing with indigenous essential oils, their composition, uses, and commercial possibilities, were contributed by the delegates at a Symposium on Research and Development of Essential Oils and Aromatic Chemicals and published by the Council of Scientific and Industrial Research.



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